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Health and Environmental Effects Profile for Bromoxynil Octanoate

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR BROMOXYNIL OCTANOATE

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16. ABSTRACT

The Health and Environmental Effects Profile for bromoxynil octanoate was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Bromoxynil octanoate has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for bromoxynil octanoate is 3×10^{-2} (mg/kg bw/day) for oral exposure.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

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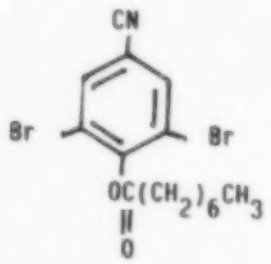
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
LD_{50}	Dose lethal to 50% of recipients
NOEL	No-observed-effect level
ppm	Parts per million

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Bromoxynil octanoate is the common name for 2,6-dibromo-4-cyanophenyl octanoate (BCPC, 1977). This compound is also known as 3,5-dibromo-4-octanoyloxy-benzonitrile, bronate, 2,6-dibromo-4-cyanopnenyl octanoate and buctril (BCPC, 1977; NIOSH, 1983). This compound was introduced in 1963 by May and Baker, Ltd. under the code numbers "MB 10,731" and "16272RP" and the trademark "Buctril" (BCPC, 1977). The structure of bromoxynil octanoate is depicted below:



Empirical formula: $C_{15}H_{17}Br_2NO_2$

Molecular weight: 403

The Chemical Abstracts Service (CAS) Registry Number for this compound is 1689-99-2.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Bromoxynil octanoate is a creamy, waxy solid. Some of the physical properties are listed below (BCPC, 1977):

Melting point:	45-46°C
Sublimes at 90°C at 0.1 torr	
Solubility at 25°C in:	
Acetone	>100 g/ℓ
Methanol	100 g/ℓ
Xylene	700 g/ℓ

Water	3.9 mg/L (calculated from log K_{ow}0
Log K_{ow} (at 25°C)	4.9 (calculated by Syracuse Research Corp.)

Bromoxynil octanoate is stable in storage and is slightly corrosive (BCPC, 1977).

1.3. PRODUCTION DATA

Bromoxynil octanoate is produced by the esterification of bromoxynil with octanoyl chloride.

Bromoxynil octanoate is an herbicide produced by Rhone-Poulenc Inc., Agrochem. Div., Portland, Oregon, and by Union Carbide Corp. Agric. Products Group, Ambler, Pennsylvania (SRI, 1983). Union Carbide produces 100,000-1,000,000 pounds annually (U.S. EPA, 1977).

1.4. USE DATA

Bromoxynil octanoate is used as a contact post-emergent herbicide to control broad-leaved annual weeds in cereals. The fact that this chemical is included in the TSCA File suggests that it may have uses other than as an herbicide.

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

The two most likely routes of entry of this herbicide into the atmosphere are spray drift during application of the herbicide to soil and evaporation from the soil after application. No information pertaining to the fate or transport of this chemical in the atmosphere was found in the available literature. The fate of bromoxynil octanoate in the air is likely to be determined by its ability to undergo reactions with O_3, NO_x and free radicals (e.g., ·OH) and by its ability to undergo photochemical reactions.

No studies relating to the transport of bromoxynil octanoate in the atmosphere were found in the available literature. It is difficult to make theoretical predictions based on the limited amount of data.

No studies pertaining to the fate and transport of bromoxynil octanoate in water were found in the available literature (see Appendix). Based on the compound's ability to undergo degradation in the soil (Smith, 1980; Collins, 1973), it can be speculated that these processes will influence its fate in the aqueous media as well.

Limited data on the fate of this compound in the soil were available. The breakdown of ^{14}C-labeled bromoxynil octanoate in five soil types was studied by Collins (1973) using a soil perfusion apparatus. The herbicide was degraded extensively at 15°C with 80% of the radioactivity in the ^{14}CN group and up to 63% of the ^{14}C in the ring liberated as CO_2 within 12-13 weeks. A portion (16-19%) of the radioactivity from the ring labeled herbicide, possibly in the form of a degradation product not readily leached, remained attached to the soil. Smith (1980) reported that bromoxynil

octanoate, when applied to moist heavy clay or sandy loam at a concentration of 0.1-05 µg/g, was quickly converted to the free phenol and rapidly degraded (>97%) within 7 days. This conversion was 80% complete in 24 hours.

No data on the transport of this herbicide in the soil were located.

3. EXPOSURE

No monitoring data for this compound were available in STORET or elsewhere in the literature cited in the Appendix.

4. PHARMACOKINETICS

Pertinent data regarding the absorption, distribution, metabolism and excretion of bromoxynil octanoate were not located in the available literature cited in the Appendix.

5. EFFECTS

Limited information regarding mutagenicity, teratogenicity, reproductive effects, and subchronic testing was found in a Federal Register article on tolerance for bromoxynil residues resulting from the use of bromoxynil octanoate or bromoxynil butyrate. Because it is unclear whether the compound tested was bromoxynil or one of the named esters and because no details were provided, this information is presented only in Section 7.1.

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of bromoxynil octanoate were not located in the available literature cited in the Appendix. This compound is not scheduled for testing by the National Toxicology Program (NTP, 1983).

5.2. MUTAGENICITY

Pertinent data regarding the mutagenicity of bromoxynil octanoate were not located in the available literature cited in the Appendix.

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of bromoxynil octanoate were not located in the available literature cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of bromoxynil octanoate were not located in the available literature cited in the Appendix.

5.5. CHRONIC TOXICITY

Pertinent data regarding the chronic toxicity of bromoxynil octanoate were not located in the available literature cited in the Appendix.

5.6. OTHER RELEVANT INFORMATION

Oral LD_{50}s were reported for the rat (250 mg/kg), the mouse (245 mg/kg), and the rabbit (2000 mg/kg) (NIOSH, 1983).

6. AQUATIC TOXICITY

Pertinent data regarding the effects of bromoxynil octanoate on aquatic organisms were not located in the available literature cited in the Appendix.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Guidelines and standards for the protection of humans from the toxic effects of bromoxynil octanoate, per se, have not been established. In 1982, in response to petitions of Union Carbide Agricultural Products Co., Inc. and Rhone-Poulenc, Inc., the U.S. EPA (Federal Register, 1982 p. 2862 and p. 55224, respectively) established a maximum permissible level of 0.1 ppm for residues of the herbicide bromoxynil resulting from the application of bromoxynil octanoate (and/or bromoxynil butyrate) in or on raw agricultural commodities. Since the tolerance level was established for residues of bromoxynil, rather than for bromoxynil octanoate (or butyrate), it is assumed that the toxicological data on which the level was based apply to bromoxynil, rather than to the octanoate (or the butyrate), although this was not clear from the two accounts (Federal Register, 1982, p. 2862 and p. 55224). The data included a 13-week feeding study in the dog with a NOEL of 5 mg/kg/day, a 13-week feeding study in the rat with a dietary NOEL of 312 ppm, a 3-generation dietary study in the rat with a NOEL of $\geq$300 ppm and a negative mutagenicity assay in Salmonella typhimurium (Federal Register, 1982, p. 2862 and p. 55224). The maximum permissible level was also based on the results of a teratogenicity study (or studies) in rats. A NOEL for teratogenic effects of 15 mg/kg/day was reported in one account (Federal Register, 1982, p. 2862), but a NOEL of >35 mg/kg for teratogenicity with fetotoxicity at >5 mg/kg was reported in the later account (Federal Register, 1982, p. 55224). The reason for the discrepancy in teratogenicity NOELs between the accounts is not apparent. Further information regarding any of these toxicological studies was not provided by U.S. EPA (Federal Register, 1982, p. 2862 and p. 55224), and these studies were not en-

countered in the available published literature. Based on the 13-week study in dogs and using an uncertainty factor of 2000, an ADI for bromoxynil of 0.0025 mg/kg/day was calculated (Federal Register, 1982, p. 2862 and p. 55224).

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of bromoxynil octanoate have not been established.

8. RISK ASSESSMENT

Pertinent data regarding the carcinogenicity of bromoxynil octanoate were not located in the available literature cited in the Appendix.

Pertinent data regarding the effects of subchronic or chronic exposure to bromoxynil octanoate were not located in the available literature. Unpublished oral teratogenicity and reproductive effects studies (rat) and unpublished subchronic feeding studies (dog and rat) were mentioned briefly in Federal Register articles that set tolerances for bromoxynil residues on raw agricultural commodities when such residues result from the use of bromoxynil octanoate (or bromoxynil butyrate) (Federal Register, 1982, p. 2862 and p. 55525). Details of the studies were not provided and it was unclear which compound was tested; however, it was assumed to be bromoxynil. Using a safety factor of 2000, an ADI of 0.0025 mg/kg/day for bromoxynil was calculated from a NOEL of 5 mg/kg day in the subchronic feeding study with dogs (Federal Register, 1982, p. 2862 and p. 55525). The adequacy of the studies, and consequently of this ADI, cannot be evaluated because no details regarding the studies were available.

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form as a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment can, however, be presented in this chapter.

The CBI Appendix to this document reviews other animal data, including a subchronic feeding study using dogs that may be the same study mentioned in

the Federal Register (1982). The CBI data indicate that a less conservative ADI should be adopted. An ADI of 0.03 mg/kg bw/day or 2.1 mg/day for a 70 kg man is recommended, based on a NOAEL of 8.6 mg/kg bw/day for elevated relative liver and kidney weights in rats in a subchronic feeding study, and an uncertainty factor of 321 (10 to account for species-to-species extrapolation, 10 for protection of unusually sensitive individuals within the population and 3.2 for the use of subchronic data to derive an ADI).

9. REFERENCES

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Collins. 1973. Perfusion studies with bromoxynil octanoates in soil. Pestic. Sci. 4: 181-192. (CA 78:123179h)

Federal Register. 1982. Volume 47.

NIOSH (National Institute for Occupational Safety and Health). 1983. RTECS (Registry of Toxic Effects of Chemical Substances). May, 1983: Online.

NTP (National Toxicology Program). 1983. Carcinogenesis Testing Program. Chemicals on Standard Protocol. Management Status Report, dated April 20, 1983.

Smith, A.E. 1980. An analytical procedure for bromoxynil and its octanoate in soils; persistence studies with bromoxynil octanoate in combination with other herbicides in soil. Pestic. Sci. 11(3): 341-346.

SRI (Stanford Research Institute). 1983. SRI, Directory of Chemical Producers, SRI International, Menlo Park, CA.

U.S. EPA. 1977. TSCA (Toxic Substances Control Act). Plant and Producer Search System. Search through CIS, May, 1983.

APPENDIX:

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE

These searches were conducted in May, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7th), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. TLVs: Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981). Cincinnati, OH. 486 p.

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Grayson, M. and D. Eckroth, Ed. 1978-1983. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., MA. 575 p.

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U.S. EPA. 1983. CHIB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

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Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.